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Identification of geographical factors associated with early spread of foot-and-mouth disease in the 2001 Uruguayan epidemic

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Objectives—To explore whether early analysis of spatial data may result in identification of variables associated with epidemic spread.

Sample population— Thirty-seven infected farms (cases) reported in the first 6 days of the 2001 Uruguayan Foot-and-Mouth disease (FMD) epidemic.

Procedure—Creation of a geo-referenced database and retrospective analysis of case location in relation to: a) farm density, b) animal density, c) farming type (beef vs. dairy production), d) road density, e) case distance to the nearest road, f) farm size, g) farm ownership and h) day of infection. Mean or median results of 1-3 day vs. 4-6 day spatial data were compared. Spatial-temporal associations were investigated by correlation analysis.

Results—Comparison of median or mean values, and correlation analysis showed increased road density, animal density and dairy farming, and decreased farm size and case distance to the nearest road over time ($P<0.05$). Based on these findings, a route that linked most cases with the shortest possible length and also considered significantly associated variables, was created. It included 86.1% of all cases reported by 60 days into the epidemic.

Conclusions and relevance—Epidemic direction can be assessed based on road density and other spatial variables as early as 6 days into an epidemic. Epidemic control areas may be more effectively identified if local spatial data are considered (which would result in territorial polygons, rather than territorial rings). Control policies may also consider farm-specific production and management risks, such as different policy for dairy than beef farm areas, if

appropriate. It is concluded that assessments of spatial data can facilitate early decision-making.

Introduction

The study of epidemic dissemination of animal diseases and, particularly, the decision-making process leading to selection of control policy has traditionally focused on biologic data. However, epidemics occur in a given space, which is not equally distributed. Rivers, mountains, cities and roads, among other factors, influence disease dissemination. Therefore, the probability of a farm to be infected during an epidemic is not the same throughout a given territory. Ignoring the effect of space may result in invalid predictions about epidemic spread.

One alternative to solve the limitations of deterministic epidemiologic assessments is to consider spatial data. That is, data on variables such as the distance among infected farms, the structure of possible means of epidemic spread (such as the road structure), or animal density in various territories. In order to be effective, that task should be completed in a short time.

Early determination of the probable direction or route toward which the infecting agent may escape is critical for cost-effective control measures. However, such assessment may be hindered by biologic phenomena. For instance, the **Foot-and-Mouth Disease** (**FMD**) virus can reproduce within 2-3 days and infected animals may become infectious (capable of disseminating the virus to other animals) even before clinical signs develop.[1] As a result, the virus may escape the original infection site before its presence is noticed. Therefore, at least two viral reproduction cycles (ie, incubation periods) need to occur in order to assess the direction(s) the epidemic follows. A compromise between a long waiting period (when abundant data can facilitate a sound decision) and the earliest possible time (when control measures are less costly) is to assess data when two incubation periods have occurred. Because time is a precious resource in epidemic control policy, in the case of FMD, a conservative estimate for two incubation periods can be set at approximately 6 days. While individual cases may experience an incubation period longer than 3 days, and delayed reporting (especially at the beginning of an epidemic) may result in additional source of bias (ie, cases reported after 3 days into the epidemic may actually represent primary cases)[2], by observing cases reported in the first 6 days it is expected that, if not all, at least some should represent secondary cases. Then, if changes in the location of cases are observed among (putative) secondary cases, a 6-day observation period may be the shortest possible interval that may identify variables associated with epidemic progression.

Geographical information systems (**GIS**) may help to achieve that task. By virtue of its capability for integrating data on points, lines and polygons, GIS is both an analytical tool and a multiplier of variables. It can create secondary variables. For example, it can measure the length of a multi-segment line (ie, a highway network) and the area of an irregular polygon (ie, a territory) and so create a secondary variable (ie, the mean of line length per unit of area [km of roads per sq km of area, or road density]). Similarly, it can find the shortest multi-segment line that connects most points (ie, a route). These features allow us to generate data on features available on graphic formats (maps) even if the original database lacks that information. GIS can also convert numerical data into graphic data. As a result, hundreds of new datasets can be generated from just a few sources of data.[3, 4] Thus, GIS-based assessments can facilitate a paradigm shift: rather than following pre-determined hypotheses, they generate a data-driven approach.

Although GIS has been applied in veterinary epidemiology before[5, 6], this tool has only once been used to evaluate diseases of rapid dissemination. That was the case of the 2001 British FMD epidemic.[4, 7, 8] However, the role of possible means of epidemic spread (such as the road network) and associated variables, has not been assessed yet.[9]

Here, the FMD epidemic that took place in Uruguay in 2001 was retrospectively analyzed to explore the role of spatial variables in relation to early epidemic spread. Data on farm density, road network structure (categorized by road density and farm distance to the nearest road), animal density (beef vs. dairy cattle), farming type (beef vs. dairy), and farm size were assessed in relation to daily cases. The purpose of this study was to identify as early as possible (after two incubation cycles of the infective agent) which variable, if any, was associated with epidemic spread.

Materials and Methods

Software—Two commercial GIS software packages were used to geo-reference available maps and to construct maps based on quantitative sources.[a]

Data sources— The basic map was a 1:500,000 scale political division geographic chart of Uruguay, kindly provided by its producer (the Geographical Service of the Uruguayan Ministry of Defense, http://www.ejercito.mil.uy/cal/sgm/frame3.htm). This map was then geo-referenced into GIS software, providing national and state border contours as well as the national highway network, cities and riverways. Data on farm density, animal density, farm size, county-level percent of farms declaring beef [or dairy] production being their principal source of income (farming type), and location of FMD-infected farms (cases) were obtained from public records of the Uruguayan Ministry of Livestock, Agriculture and Fisheries (MGAP, http:www.mgap.gub.uy) and MGAP's Directorate of Agricultural Statistics (DIEA). In particular, the 2000 Annals and 2000 Agricultural Census provided space-related farming data (http://207.3.127.35/Diea/anuarios.htm, http://207.3.127.35/Diea/default.htm).

Scale of the selected variables—Four scales of data were used: a) multi-state, b) state, c) county, and d) local (farm). Multi-state data included: i) highway network, and ii) distance of every point in the territory to the nearest road. State-level data included: i) animal density (number of beef and dairy cattle heads per sq km), ii) farm density (number of county farms per county area [sq m]), and iii) farm size (percentage of farms of >500 hectares). County-level data included: i) farm type (income attributed to beef vs. dairy production, as reported by farmers), ii) road density, and iii) county area. Local (farm-level) data included: i) point location of farms infected in the first 6 days of the epidemic; ii) when available, farm ownership or fragmentation (single-parcel or multi-parcel holdings); iii) when available, size (has.) of farms infected in the first 6 days of the epidemic; and iv) location of farms infected between days 7 and 60 of the epidemic.

Methods—A series of spatial layers (containing both graphic and numerical data) was built. The foundational layer contained country, multi-state, state and county level surface data (polygons). Further layers included multi-state highway network (lines), and point data on farm location, daily cases of the first 6 days (first day: April 23, 2001), and cases reported between 7 and 60 days into the epidemic. Secondary variables were created by GIS by linking state-level animal density (animals per sq km) and farm size (hectares) from the 2000 Uruguayan

Agricultural Census (MGAP-DIEA, 2000 Censo Agropecuario) with state area data (generated by the same software). Municipal-level (county) secondary variables were generated in the same fashion (ie, road density [kilometers of road per square kilometer of county area]. The probable infection route was identified as follows. After selecting the highway network shapefile, the ArcView GIS *Network* command is chosen from the menu, and the *Find Closest Facility* window is open. Within this window, the point coverage file that reports case location and the *Travel from event* window are then selected. A *cutoff cost* determined by the operator (ie, 250 km) is then typed. The number of *facilities to find* (the number of infected farms recorded in the point coverage on case location) is also indicated (37 in this study). Once the analysis is run, the same *Facilities* window will report the number of events encountered. An *event* is a dead-end point on the road network. Since any *event* (ie, any case occurring within one viral incubation period) could be the actual primary case, it is convenient to re-calculate the *facility* network analysis starting on each one of those. This allows the operator to determine whether the epidemic progression pattern varies significantly if another primary *event* (possible primary case) is considered (ie, to assess if all cases are reached by the resulting "infection routes" and, if so, whether different solutions vary significantly in route length).

Study area —The Southwestern portion of the Uruguayan territory, of approximately 74,945 sq km, was selected for evaluation of spatial variables (**Fig 1A**). In this region, on April 23, 2001, an epidemic of FMD was first reported (**Fig 1B**).

Statistical analyses—Comparison of means or medians of the (estimated) first incubation or reproductive cycle of the infective agent (first 3 days) vs. those of days 4 to 6 were made by either use of the Student's *t* test or the Mann-Whitney test, respectively. Spatial-temporal associations were assessed by correlation analysis. Statistical tests were performed using a commercial package.[b] For all tests, $P<0.05$ was considered significant.

Results

Summary data— In order to assess epidemic spread as early as possible, infected farms (cases) reported in the first 6 days of the epidemic were investigated. It was reasoned that within this interval, approximately two viral incubation cycles could have occurred and their data could indicate the direction or territory of epidemic spread. Data on 37 of the 59 cases reported in the first 6 days of the infection were obtained and geo-referenced (**Table 1**).

Farm density—The state farm density (number of state farms/state area [sq km[) associated with cases changed significantly over the 6-day interval under study (**Fig 2A**). The median state farm density in the first 3 days was 0.226 farms/sq km, and doubled in the second 3-day period (0.528 farms/sq km, P =0.02). Farm density was positively correlated with infection time, road density, and dairy farming rank; and negatively associated with case distance to the nearest road, beef farming rank, farm size and both dairy and beef density (**Table 2**).

Road network—County road density (km of road/county area [sq k]) increased as the time of the epidemic increased (**Fig 2B**). In the second half of the studied period road density was almost twofold higher than in the first 3 days (medians: 0.146 vs. 0.080, respectively, P =0.005). Road density was positively associated with dairy farming rank and both dairy and beef density, and negatively correlated with beef farming rank and farm size (**Table 2**).

Case distance to the nearest road—Twenty-eight of the 37 cases (75.6%) were located within 5 km from the highway network (**Fig 3**). CDNR appeared to be negatively correlated with infection time, although it did not reach statistical significance. At 4-6 days into the epidemic, median CDNR (1288 m) was significantly reduced compared to that of the first 3 days (4387 m, P=0.023). CDNR was significantly and negatively correlated with road density, farm density, and dairy density, and appeared also to be negatively associated with dairy farming rank, although it did not reach statistical significance. In contrast, CDNR increased significantly as the importance of beef farming increased (**Table 2**).

Animal density— The region under analysis showed marked differences in bovine (beef and dairy) density (**Fig 4**). Both beef and dairy densities (state number of heads per sq km) associated with cases were positively correlated with time (**Table 2**). When compared in 3-day periods, beef density did not change significantly (**Table 1**). In contrast, the median dairy density (6 heads per sq km at day 1-3) almost tripled in the second half of the investigated period (19.5 heads per sq km, P=0.002). Dairy and beef density showed identical associations with the other variables. Both were positively associated with road density, farm density, and dairy farming rank, and negatively associated with beef farming rank (**Table 2**).

Farming type ranks— Farming type (expressed as dairy or beef farming rank) indicated that lower beef and higher dairy ranks were associated with epidemic time (**Fig 5A, B**). Beef farming rank decreased as farm density and road density increased (variables both positively associated with epidemic progression, **Table 2**). A negative correlation between beef farming rank and beef animal density suggested that beef-based farm income was a rather extensive farming practice. This observation was further supported by significant positive correlations between beef farming rank and CDNR as well as beef farming rank and farm size (**Table 2**), which indicate that beef-based predominant income is associated with rather large farms located in areas where individual farms tend to be far from the nearest road. In contrast, dairy farming rank was positively associated with dairy animal density, road density and beef animal density, and negatively correlated with farm size and beef farming rank, which supports the view that intensive farming (the farming type that includes smaller farms and higher road-dependent contacts) is associated with either dairy or mixed farming and more prone to become infected. In agreement with this expectation, a higher mean dairy farming rank was observed in the second (2.33 ± 1.33) than in the first 3-day period (1.714 ± 0.75, P=0.049), while a lower median beef farming rank (3) occurred in the second than in the first 3-day interval (4, P=0.03).

Farm size and farm fragmentation— Although data were only available for 28 of the 37 cases, farm size associated with cases appeared to decrease over time. The median size of 1-3 day infected farms was 988 hectares while that of 4-6 day cases was 600 has (P=0.036). An additional measure of farm size (the percentage of state farms of 500 has or more) was assessed (**Fig 6**). This measure decreased from 7.1 (median for 1-3 day cases) to 5.5 at 4-6 days (P=0.005). Farm size was positively correlated with beef farming and negatively correlated with dairy farming rank (**Table 2**). Although data were incomplete, management-related risks were suggested by the fact that 16 of 27 infected farms (59%) reported fragmented farms (multi-parcel ownership, **Table 1**). However, the proportion of multi-parcel ownership over time remained unchanged.

Construction of a probable infection route—The second phase of the analysis attempted to identify the area of probable epidemic spread. Correlation analysis of daily data indicated that as time increased, so did road density, farm density, animal density (both beef and dairy heads per sq km), and dairy farming rank, whereas farm size and beef farming rank decreased (**Table 2**). Consequently, a route was constructed in order to meet three criteria. This route should: i) result in the shortest path connecting most of the first 6-day cases (the lowest possible distance "cost" per case); ii) be no more than 19-km in width, in order to include the maximum case distance to the highway network observed in the first 6-day cases (18 km); and iii) consider the variables previously identified.

The preliminary solution resulted in a 930-km long and 19-km wide route that connected 36 of the 37 cases observed in the first 6 days. One case, while located 8061 meters away from the highway network, was excluded because: a) its inclusion would increase excessively the route length (it would have an individual "cost" of 62 km, while the average "cost" of the remaining 36 cases was just 930/36 or 25.7 km per case); and b) that case was located in an area where most farms (> 80%) were dedicated to beef production (predictor negatively associated with epidemic spread, **Fig 7a**). The final step included areas of road density greater than 0.1 km/sq km, where rather intensive farming predominate. This solution included 86.1% (1150 of 1335) of all cases reported by the 60th day of this outbreak (**Fig 7b**).

Discussion

While the geo-referenced data here presented is the product of integrating data from several public sources, this dataset should not be construed as necessarily representing the epidemic that took place in Uruguay in 2001. Rather, it should be perceived as a likely scenario where an epidemic occurs. Yet, that scenario (as usually found in epidemics) may lack data potentially relevant or contain incomplete (or outdated) data. For example, animal data considered for this analysis were those of the 2000 Agricultural Census, not necessarily identical to the data corresponding to April 23-June 23, 2001, timeframe of this analysis. Similarly, this database lacks information on weather conditions (i.e., wind). Therefore, this discussion should only be regarded as a relational analysis of the variables here presented.

The 2001 Uruguayan FMD epidemic infected mainly bovines. It began in a rather isolated area where beef farming was the principal activity. Later, it spread toward areas of greater farm, animal and road density, where dairy and mixed farming tended to predominate. These findings suggest that the road structure may be a significant variable associated with epidemic spread. The highway structure concept was here operationalized with two constructs: county road density, and case distance to the nearest road (CDNR).

Since road density increased and CDNR decreased significantly over time while CDNR and road density were negatively correlated, a plausible hypothesis consistent with these three relationships is that at the early epidemic stage the virus disseminated taking advantage of the road network which resulted in regional or "along roads" spread. Thus, high road density may initially be instrumental to facilitate medium to long-distance infections. In such case, the chances of a given farm to be closer to the nearest road becomes greater as road density increases, which explains the negative correlation observed between road density and CDNR. Later (when road blocks are in place), epidemics may spread perpendicularly to road lines.

A two-phase epidemic spread process has been suggested before.[7, 8, 10] It can be described as an initial, "forward" or "along roads" spread phase, followed by a "lateral" or "away from roads" phase. As a result, road-dependent case occurrence ("progenitor cases") may result in rather few cases as percentage of total number of cases but more relevant predicting spatial spread, whereas secondary ("daughter") cases may represent a larger percentage of total number of cases but account less for spatial spread. These two epidemic phases may occur at the same time (ie, viral "escapes" may result in new "first phases" even late into an epidemic). In this study, road density increased over time, which suggests that the interval under analysis represented the earliest of those phases.

Yet, the purpose of this study was not to assess the two-phase epidemic spread hypothesis (which, very likely, could require a larger interval) but to assess epidemic data in order to facilitate decision-making. In spite of the short timeframe analyzed, statistically significant differences were observed.

Based on the first phase of the analysis, it was expected that the epidemic would spread toward regions of greater road density, farm density, animal (beef and dairy) density and dairy farming. In spite of not considering one of the reported cases, the constructed region of probable epidemic spread included 86.1% of the cases observed over a 2-month period.

Dairy farms appeared to experience greater FMD case incidence. One plausible explanation may relate to greater direct contacts associated with dairy farming. Previous reports have indicated that dairy farms have an approximately 4-fold greater contact rate than beef farms and/or concluded that milk trucks may disseminate epidemics.[11, 12] Traffic density is usually higher in regions of greater farm, human and road density (as occurs in Uruguay's Southwest). It is then plausible that dairy farms are at greater risk because they are exposed to a greater traffic environment. Yet, later cases were also associated with high beef cattle density.

Findings also support the hypothesis that farming type (principal source of income reported by farmers) may be a more comprehensive predictor than animal density alone. For instance, a farm composed of 40 % dairy cattle and 60% beef cattle might be regarded as a "beef" farm if animal density is considered but as a "dairy" farm if such is its principal income. Thus, this variable may become a richer measure to estimate direct (animal density-dependent) and indirect (production-dependent) farm risk. However, it may also conceal a bias. Farming type may be a subjective identifier if it is solely based on farmer's perception. For example, in this study two counties reported farming (beef and dairy) ranks that, together, exceeded 100%. These errors illustrate the importance of epidemic data quality, which, due to the multiplicative nature of GIS analytical approaches, can expand the magnitude of invalid inferences.

These findings suggest the need for differentiating several concepts associated with traffic as they relate to epidemic spread. The first relates to farm-to-farm contacts (direct contacts) such as animal trade. The second concept (indirect contacts) would involve those ending in a farm through another means (ie, vehicles). Local traffic density can influence both direct and indirect contacts. Traffic density may be a function of road density and traffic intensity. The greater the county road density, the greater the chances of acquiring a disease through direct or indirect contacts. However, its associated variable, the mean of vehicles traveling in a given road segment on an average period (or traffic intensity) may differ from road density (ie, road density may be high and the actual traffic low or vice versa). It is suggested that future studies may assess the role of traffic intensity on epidemic spread.

In this epidemic the average size of infected farms decreased over time while farm density increased. Previous studies have reported that large farms tend to be infected in the early stage of an epidemic.[7, 13] Later, as the number of large susceptible farms decreases faster than the number of smaller susceptible farms (which usually are located in areas of greater road density and higher contacts), smaller farms tend to be at higher risk.

Early identification of a plausible infection route could lead to different production and/or management-specific measures. For example, extensive beef production areas (apparently less likely to contract the disease in the scenario under analysis) could have been subject to different control measures than those applied to dairy and mixed farming areas. Similarly, fragmented farms (multi-parcel ownership) might require different control measures.

These findings may be applicable to develop space-specific control measures. Typical measures (such as ring vaccination and ring culling) consist of territorial rings centered on an infected farm.[14, 15] However, the diameter of a control area has usually been determined without consideration on local spatial data, which may lead to either excessive or insufficient policies. While reports on ring culling/vaccination have acknowledged the importance of the spatial structure[5, 10], to the best of our knowledge no one has empirically determined the polygon (rather than the circle) of territory selected to implement control measures. It is suggested that future studies should compare epidemic models using polygons rather than circles.

GIS-based models cannot generate long-term predictions nor their findings are generalizable. Had the index case occurred elsewhere, the epidemic progression would likely have followed a different pattern. Given the dynamic nature of epidemics, deterministic models can neither predict long-distance transmission events (smallworld-like contacts), nor the epidemic tail.[9, 16] In addition, they are susceptible to unpredictable changes (ie, weather related). At best, deterministic models may have an impact on short-term predictions.[9] This study showed that identification of spatial variables associated with epidemic spread can be completed within a few days after the epidemic onset. Six days were enough to identify spatial features associated with epidemic spread. While cases reported in such a short interval are likely to be under-estimated and/or delayed reporting may occur, provided that the number of cases is relatively large, a GIS-based analysis of early epidemic data may result in context-specific decision-making. In contrast, epidemiological control policy has historically been adopted at much later times.[12] Since the efficacy of this approach depends on previous data collection, anticipatory construction of databases that include geographic, demographic, management, climatic and biological variables, is recommended.

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Footnotes

[a] Arc View GIS 3.2 and Arc View 8.0, ESRI, Redlands, CA.

[b] Minitab 12.2, Minitab, State College, PA.

Legends

Figure 1—The 2001 FMD Uruguayan epidemic. A: Map of Uruguay indicating the territory considered for this analysis, which includes the site (star) where a FMD epidemic began on April 23, 2001. The four Southwestern coastal states (whose territory is completely included in the study area and all reported 2 or more cases in the period under study) include 12,396 farms, which represent approximately one-fourth (47,735) of all farms in the country. At 6 days into the epidemic, the proportion of infected farms in those states varied from 1.5 ‰ (Paysandú, the northern most state included in the study area) to 7.5 ‰ (Soriano, where the first case was reported). The other states reported 4.0 ‰ (Colonia, the Southwestern most state) and 1.7 ‰ (Río Negro, the remaining state). Source: *Censo Agropecuario 2000* (Uruguayan Ministry of Agriculture [http://207.3.127.35/Diea/anuarios.htm, http://207.3.127.35/Diea/default.htm]). B: weekly new number of cases (infected farms). Source: PAHO-PanAmerican Footh-and-Fouth Disease Center, Rio de Janeiro, Brasil [http://www.panaftosa.org.br/novo/).

Figure 2— Geo-referenced location of farm density, highway network and epidemic progression. A: State farm density (number of state farms/state area [sq km]). B: Highway network. Sources: the Uruguayan Ministry of Livestock, Agriculture and Fisheries (MGAP) and maps of the Uruguayan Geographic Military Service.

Figure 3—Distances to nearest road and epidemic progression. Results show the case (infected farm) distance and the distance of every point in the territory to the nearest road (meters).

Figure 4— Bovine density and epidemic progression. Results show the state number of bovines per state area (sq km).

Figure 5— County farming type and epidemic progression. Ranks express the percentage of county farms indicating beef or dairy production as principal source of income.

Figure 6—Farm size and epidemic progression. Results show the percentage of state farms 500 has. or larger.

Figure 7— Probable infection route. A: Preliminary 930-km long and 19-km wide route that connects 36 of the 37 cases reported in the first 6 days is depicted. One case (located in the Northeastern quadrant) is not included because it would increase in 60 km its length and is located in an area not predicted to be significantly associated with epidemic spread. Line width represents the road density of counties connected by that route (thin or wide line: less or more than 0.1 km/sq km, respectively). B: Adjusted probable infection route. It includes areas of road density greater than 0.1 and excludes farming areas of beef rank 5 (at least 81% of the farms declare beef production to be their principal income). As a validation of this route, the location of 1335 cases reported between 7 and 60 days of epidemic, of which 1150 (or 86.1%) are within the infection route, is indicated (dots).

Table 1. Identifiers of 37 farms reported infected in the first 6 days of the 2001 Uruguayan FMD epidemic

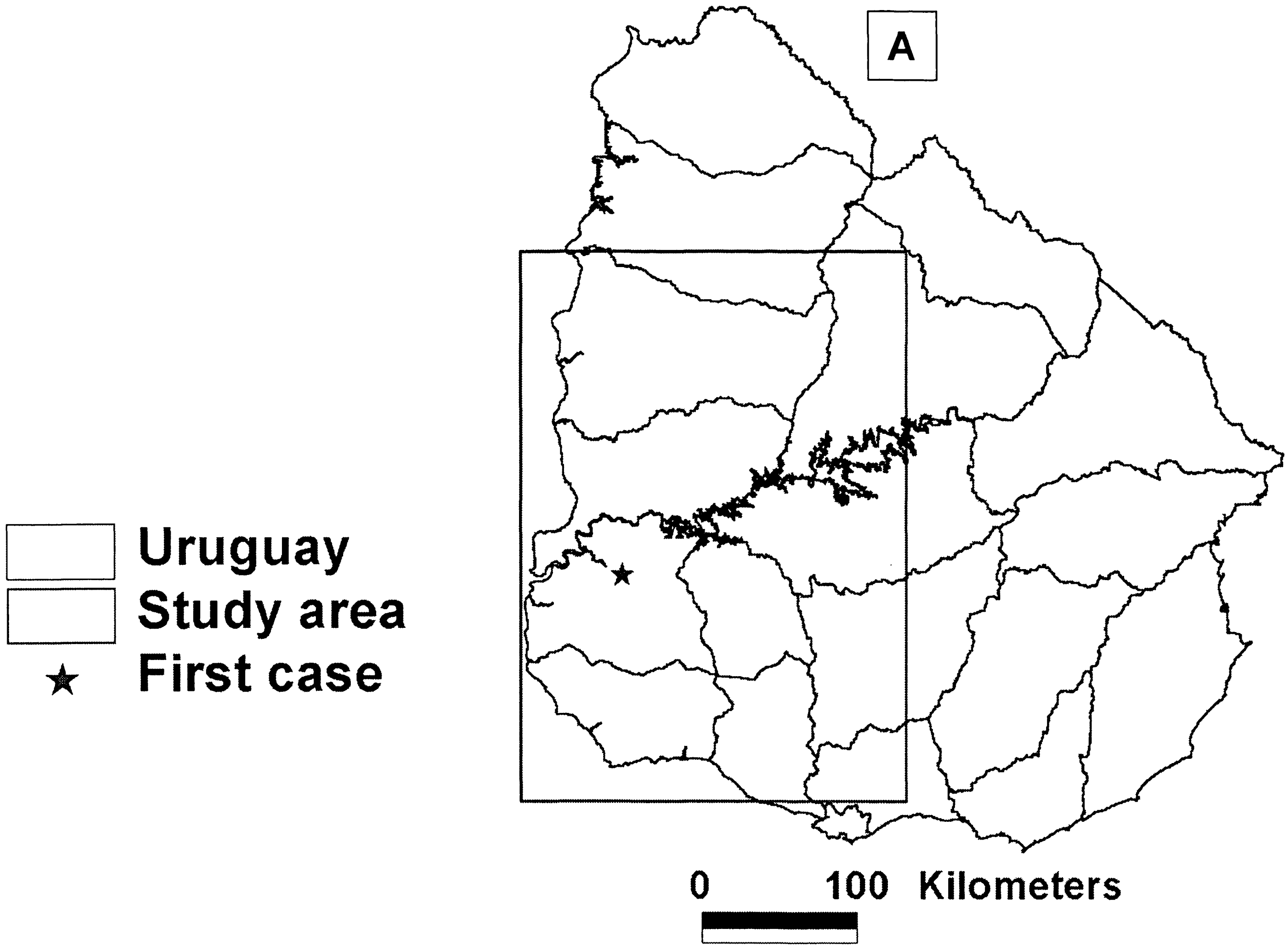
Cumulative number of cases	Infection Day	Case distance to nearest road (meters)	County road density (km/ sq km)	State farm density (farms/ sq km)	County dairy farming rank†	County beef farming rank†	State dairy density (heads/ sq km)	State beef density (heads/ sq km)	Farm size (has)	State farms >500 has (%)	Farm fragmentation
1	1	1829	0.093	0.226	2	4	6	70	534	7.1	M
2	2	1274	0.137	0.226	3	4	6	70	714	7.1	M
3	2	5754	0.080	0.144	1	4	2	49	NA	25.1	NA
4	2	7438	0.080	0.144	1	4	2	49	1236	25.1	M
5	2	3554	0.093	0.226	2	4	6	70	988	7.1	S
6	3	4387	0.068	0.226	2	4	6	70	NA	7.1	NA
7	3	8071	0.061	0.126	1	5	5	62	3162	18.0	S
8	4	1379	0.133	0.226	3	3	6	70	NA	7.1	NA
9	4	878	0.268	0.226	2	3	6	70	104	7.1	NA
10	4	1501	0.099	0.528	1	4	25	76	NA	5.5	NA
11	4	801	0.414	0.528	2	2	25	76	335	5.5	S
12	4	4462	0.159	0.528	3	3	25	76	688	5.5	S
13	4	4118	0.080	0.144	1	4	2	49	1431	25.1	S
14	4	1094	0.250	0.635	1	2	12	54	NA	1	NA
15	4	1245	0.099	0.528	1	4	25	76	NA	5.5	NA
16	5	1218	0.268	0.226	2	3	6	70	NA	7.1	NA
17	5	5385	0.141	0.226	1	4	6	70	295	7.1	M
18	5	219	0.213	0.528	2	2	25	76	145	5.5	S
19	5	2238	0.161	0.528	3	3	25	76	NA	5.5	NA
20	5	177	0.413	0.528	5	1	25	76	55	5.5	S
21	5	7020	0.067	0.126	2	4	5	62	711	18.0	S
22	5	1331	0.093	0.226	2	4	6	70	499	7.1	M
23	5	7150	0.093	0.226	2	4	6	70	NA	7.1	NA
24	5	2807	0.152	0.273	2	3	14	68	1910*	16.2	M
25	5	211	0.102	0.273	3	2	14	68	1910*	16.2	M
26	5	17896	0.093	0.226	2	4	6	70	934*	7.1	M
27	5	12791	0.068	0.226	2	4	6	70	934*	7.1	M
28	5	13965	0.068	0.226	2	4	6	70	934*	7.1	M
29	5	3155	0.105	0.226	2	4	6	70	882	7.1	S
30	6	118	0.278	0.528	1	1	25	76	551	5.5	M
31	6	1172	0.308	0.528	3	3	25	76	127	5.5	M
32	6	1106	0.295	0.528	3	2	25	76	656	5.5	M
33	6	1047	0.231	0.528	5	3	25	76	154	5.5	M
34	6	2745	0.159	0.528	3	3	25	76	600	5.5	M
35	6	807	0.256	0.528	3	3	25	76	344	5.5	S
36	6	951	0.084	0.528	3	3	25	76	959	5.5	M
37	6	135	0.084	0.528	3	3	25	76	132	5.5	S
Sub-totals‡											
7	1-3	4387	0.080	0.226	2.0	4.0	6.0	70	988	7.1	
30	4-6	1288	0.146	0.528	2.0	3.0	19.5	73	600	5.5	

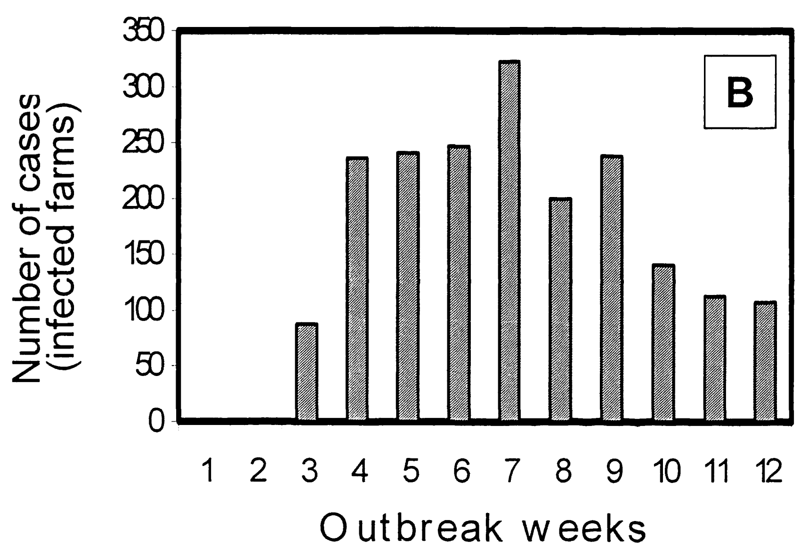
† County farming type ranks (1-5), where less than 20% (rank 1) or more than 80% (rank 5) of the farms report beef (or dairy) farming to provide their principal source of income. M: multi-parcel ownership (fragmented farm). NA: not available. S: single-parcel ownership (non-fragmented farm). *: all parcels assumed to be of equal size. ‡Sub-totals display the cumulative number of cases at 3 and 6 days into the epidemic and the medians of spatial variables.

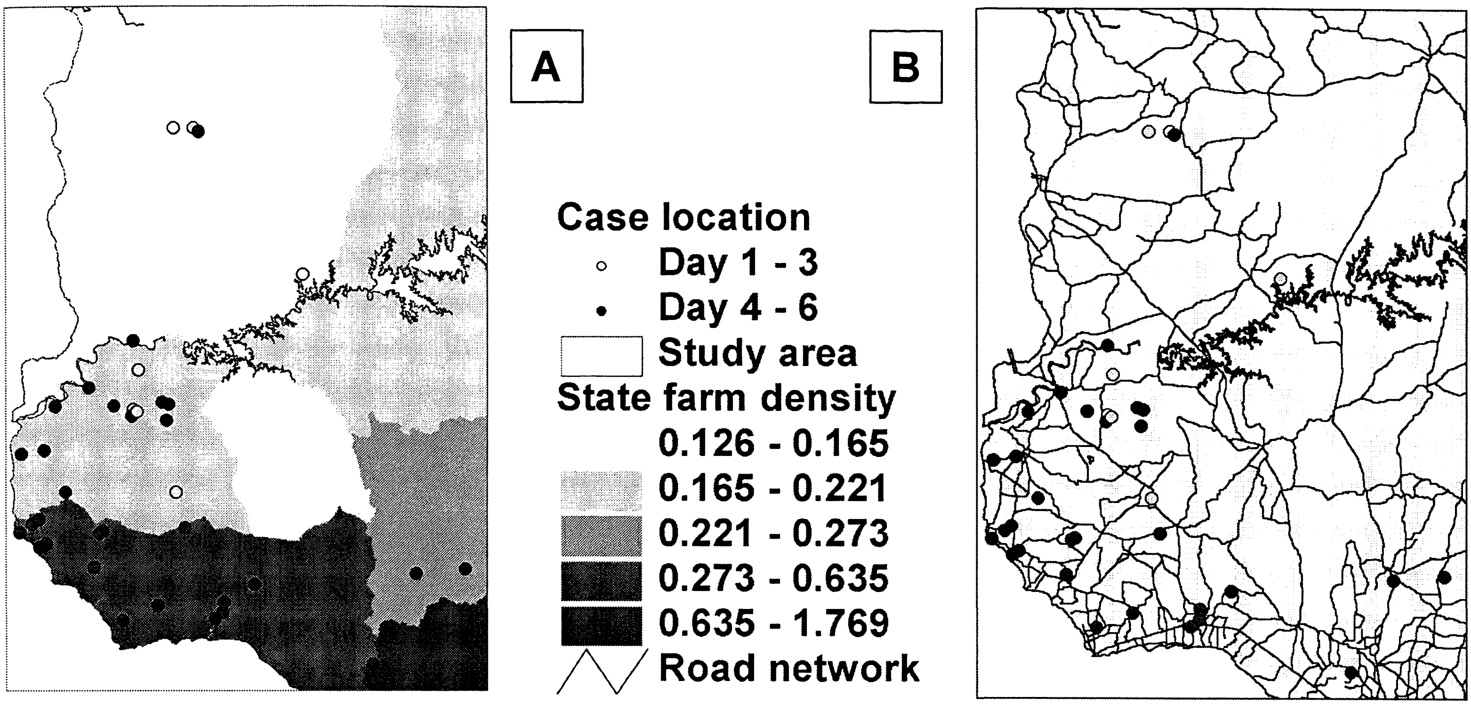
Table 2. Correlation matrix of epidemic and spatial variables

	Infection time (day)	Road density	CDNR	Farm density	Dairy farming rank	Beef farming rank	Dairy cattle density	Beef cattle density	Farm size
Infection time (day)	1								
Road density	0.81 (0.049)#	1							
CDNR	-0.75 (0.142)	-0.49 (0.002)	1						
Farm density	0.50 (0.002)	0.60 (<0.001)	-0.58 (0.001)	1					
Dairy farming rank	0.63 (0.177)	0.39 (0.017)	-0.29 (0.084)	0.38 (0.02)	1				
Beef farming rank	-0.80 (0.053)	-0.78 (<0.001)	0.55 (<0.001)	-0.67 (<0.001)	-0.42 (0.010)	1			
Dairy cattle density	0.56 (<0.001)	0.53 (0.001)	-0.52 (0.001)	0.94 (<0.001)	0.46 (0.004)	-0.63 (<0.001)	1		
Beef cattle density	0.52 (0.001)	0.37 (0.023)	-0.31 (0.063)	0.59 (<0.001)	0.53 (0.001)	-0.36 (0.027)	0.70 (<0.001)	1	
Farm size	-0.38 (0.019)	-0.41 (0.012)	0.26 (0.114)	-0.64 (<0.001)	-0.37 (0.025)	0.36 (0.027)	-0.52 (0.001)	-0.79 (<0.001)	1

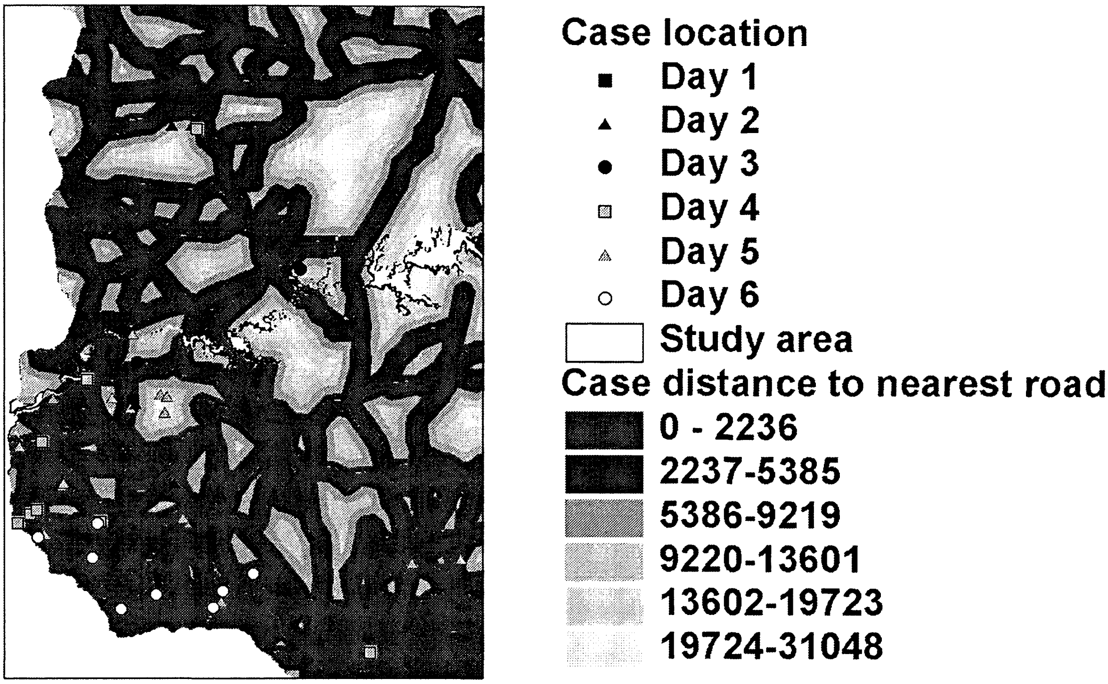
#: Road density is square-transformed (km of county road per sq km of area). CDNR: case distance to the nearest road. Cells indicate the correlation and the *P* value (within parenthesis), respectively. Variable units are those reported in Table 1.

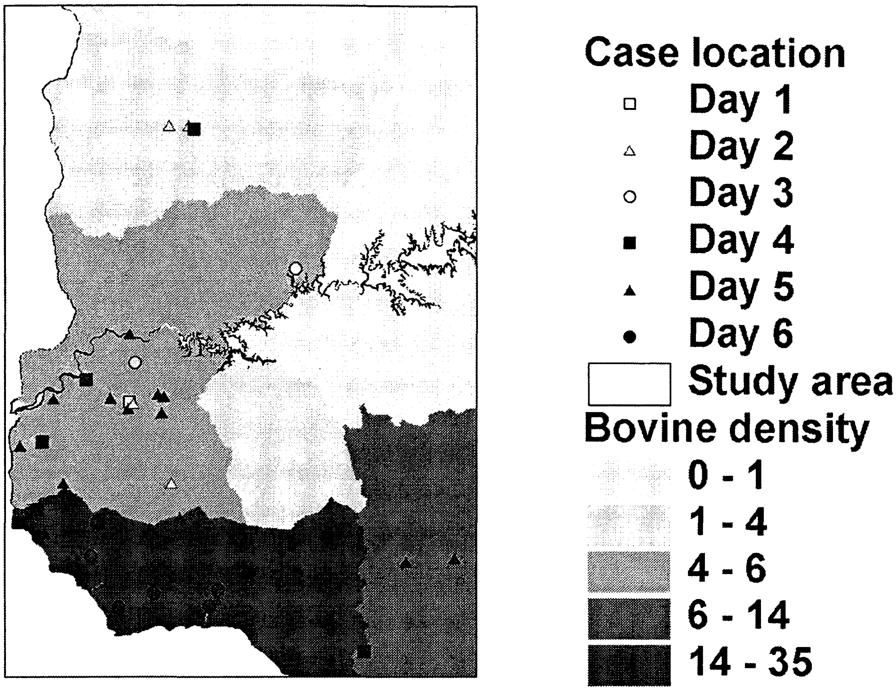

A
Uruguay
Study area
First case
0
100
Kilometers

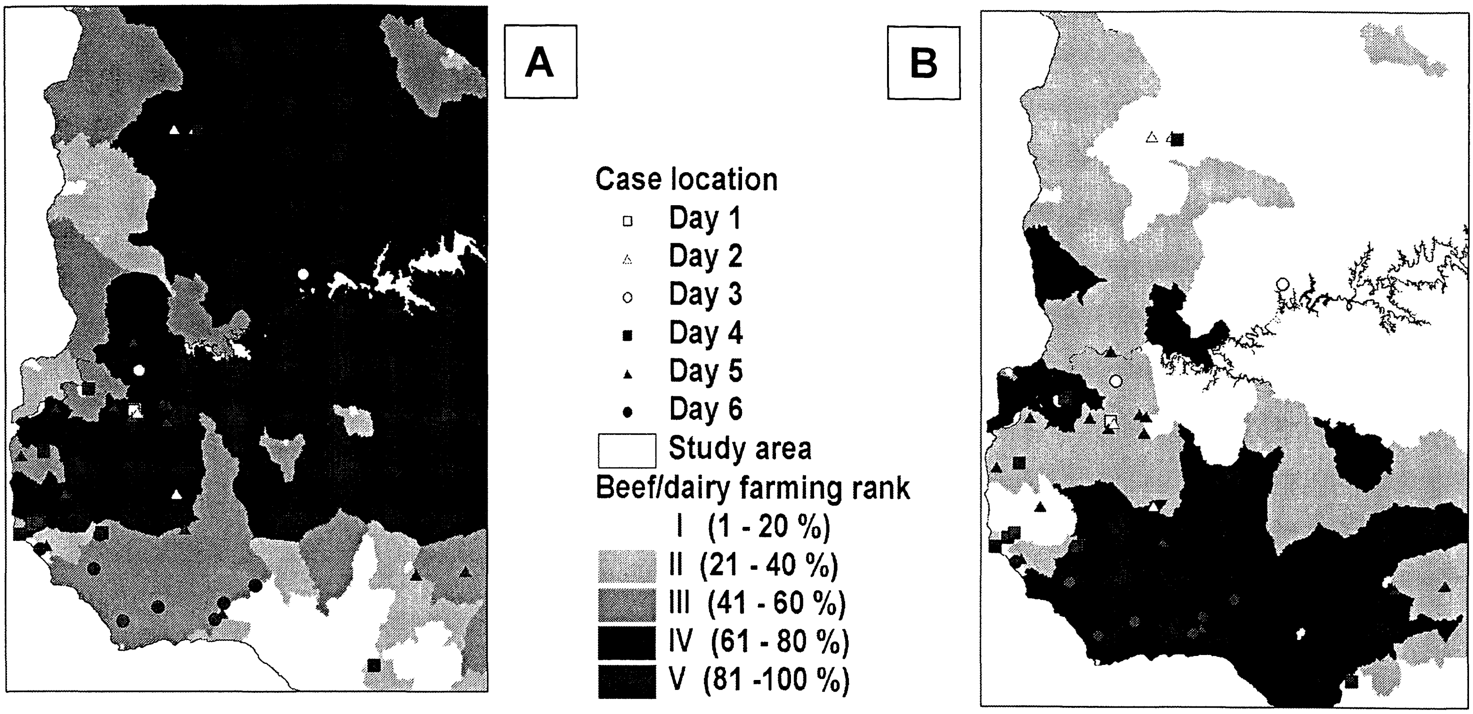

B
Number of cases
(infected farms)
350
300
250
200
150
100
50
0
1
2
3
4
5
6
7
8
9
10
11
12
Outbreak weeks

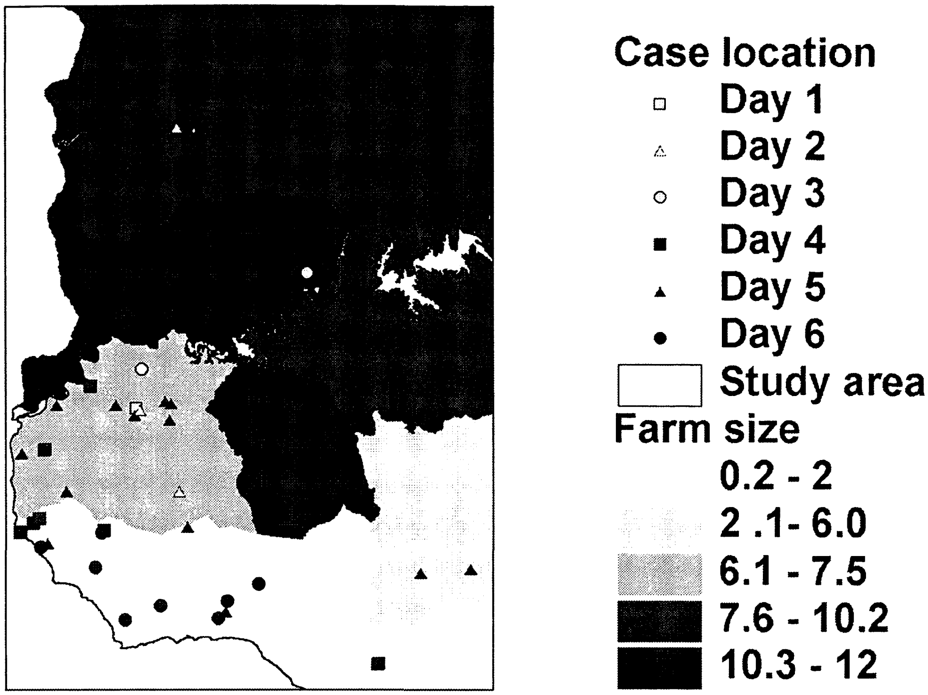


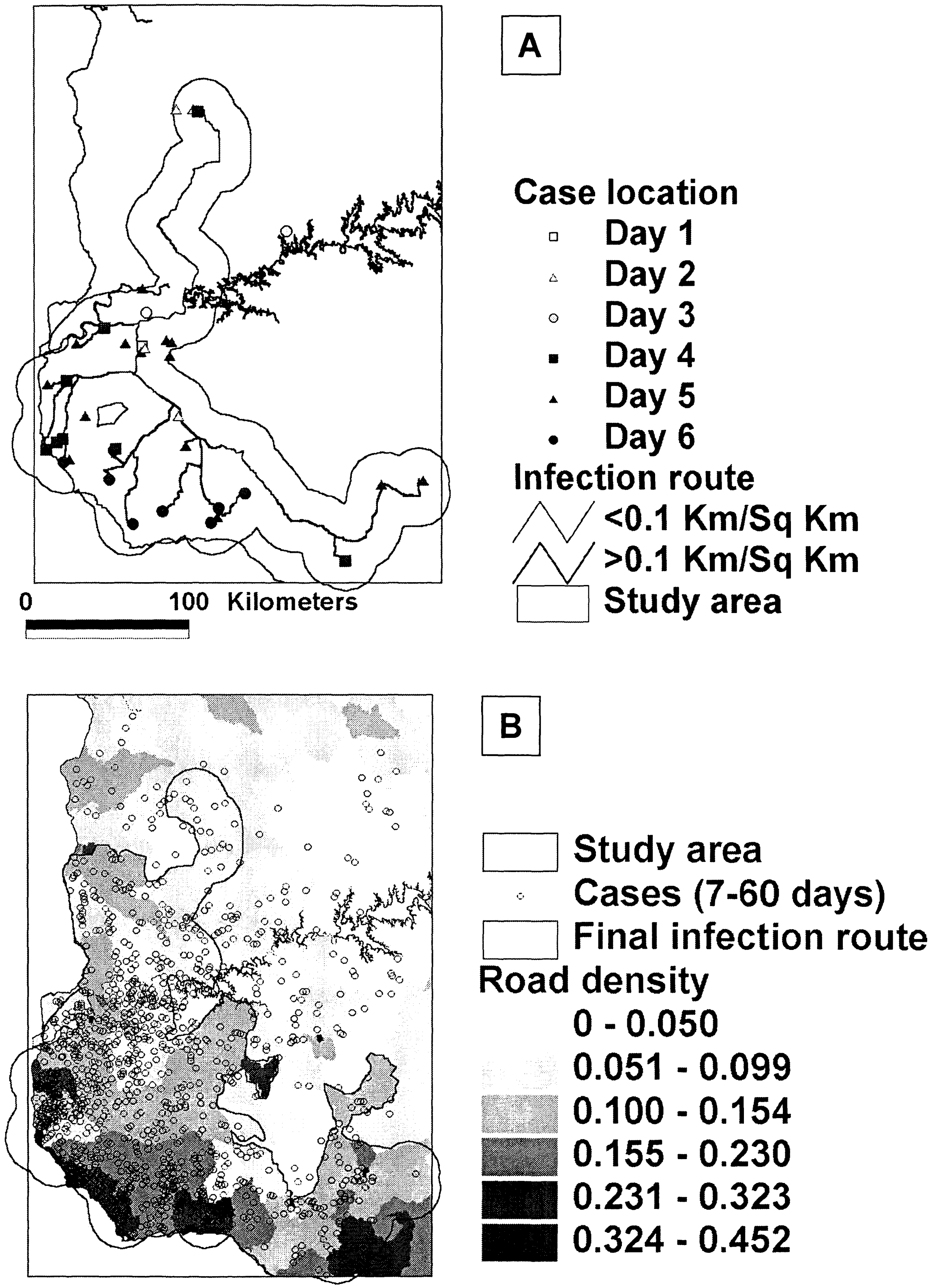
A
B
Case location
Day 1 - 3
Day 4 - 6
Study area
State farm density
0.126 - 0.165
0.165 - 0.221
0.221 - 0.273
0.273 - 0.635
0.635 - 1.769
Road network


Case location
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Study area
Case distance to nearest road
0 - 2236
2237-5385
5386-9219
9220-13601
13602-19723
19724-31048


Case location
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Study area
Bovine density
0 - 1
1 - 4
4 - 6
6 - 14
14 - 35


A
B
Case location
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Study area
Beef/dairy farming rank
I (1 - 20 %)
II (21 - 40 %)
III (41 - 60 %)
IV (61 - 80 %)
V (81 -100 %)


Case location
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Study area
Farm size
0.2 - 2
2 .1- 6.0
6.1 - 7.5
7.6 - 10.2
10.3 - 12


A
Case location
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Infection route
<0.1 Km/Sq Km
>0.1 Km/Sq Km
Study area
0
100 Kilometers
B
Study area
Cases (7-60 days)
Final infection route
Road density
0 - 0.050
0.051 - 0.099
0.100 - 0.154
0.155 - 0.230
0.231 - 0.323
0.324 - 0.452